Chapter 9
Nucleic Acids: How Structure Conveys Information

SUMMARY

Section 9.1

- The two principal kinds of nucleic acids are DNA and RNA.
- The primary structure of nucleic acids is the order of bases. The secondary structure is the three-dimensional conformation of the backbone. The tertiary structure is the supercoiling of the molecule.

Section 9.2

- Two kinds of nitrogen-containing nucleobases, pyrimidines and purines, are joined to sugars to form nucleosides.
- The sugar is deoxyribose in DNA and ribose in RNA.
- Addition of phosphate groups to nucleotides gives rise to nucleotides, which are the monomers of nucleic acids.
- When nucleotides are joined by phosphodiester bonds, they form a sugar-phosphate backbone, giving rise to DNA and RNA.
- The sequence of bases is a very important feature of the primary structure of nucleic acids, because the sequence is the genetic information that ultimately leads to the sequence of RNA and protein.

Section 9.3

- The double helix is the predominant secondary structure of DNA. The sugar–phosphate backbones, which run in antiparallel directions on the two strands, lie on the outside of the helix. Pairs of bases, one on each strand, are held in alignment by hydrogen bonds.
- The base pairs lie in a plane perpendicular to the helix axis in the most usual form of the double helix, but there are variations in structure.
- The tertiary structure of DNA depends on supercoiling. In prokaryotes, the circular DNA is twisted before the circle is sealed, giving rise to supercoiling. In eukaryotes, the supercoiled DNA is complexed with proteins known as histones.

Section 9.4

- The two strands of the double helix can be separated by heating DNA samples. This process is called denaturation.
- DNA denaturation can be monitored by observing the rise in ultraviolet absorption that accompanies the process.
- The temperature at which DNA becomes denatured by heat depends on its base composition; higher temperatures are needed to denature DNA rich in G-C base pairs.

Section 9.5

- Four kinds of RNA—transfer RNA, ribosomal RNA, messenger RNA, and small nuclear RNA—are involved in protein synthesis.
- Transfer RNA transports amino acids to the sites of protein synthesis on ribosomes, which consist of ribosomal RNAs and proteins.
- Messenger RNA directs the amino acid sequence of proteins. Small nuclear RNA is used to help process eukaryotic mRNA to its final form.
- RNA interference, which requires short stretches of siRNA, exerts control over gene expression.

LECTURE NOTES

Much of the material in this chapter will be familiar to students in the sense that the double helix and related concepts are discussed in other courses; however, some of the details are likely to be new for them. This chapter will require one to two lectures, dependent upon the level of knowledge already possessed by students.

LECTURE OUTLINE

I. Hierarchical structure of nucleic acids
II. Structures of nucleotides
    A. Purines and pyrimidines
    B. nucleosides and nucleotides
    C. Phosphodiester bonds
III. DNA structure
    A. The double helix
        1. Strand complementarity
        2. Major and minor grooves
    B. Conformational variations
        1. A-, B-, and Z-DNA
        2. Base stacking and propeller twists
    C. Supercoiling
        1. Prokaryotic supercoiling – topoisomerases and gyrase
        2. Eukaryotic supercoiling – chromatin, histones, nucleosomes
    D. DNA denaturation
IV. RNA structures and functions
    A. Sequence dependence on DNA
    B. Transfer RNA
    C. Ribosomal RNA
    D. Messenger RNA
    E. Small nuclear RNA
    F. RNA interference

ANSWERS TO PROBLEMS

9.1 Levels of Structure in Nucleic Acids

1.

(a) Double-stranded DNA is usually thought of as having secondary structure, unless we consider its supercoiling (tertiary) or association with proteins (quaternary).

(b) tRNA is a tertiary structure with many folds and twists in three dimensions.

(c) mRNA is usually considered a primary structure, as it has little other structure.

9.2 The Covalent Structure of Polynucleotides

2. Thymine has a methyl group attached to carbon 5; uracil does not.

3. In adenine, carbon 6 has an amino group attached; in hypoxanthine, carbon 6 is a carbonyl group.

4.

A	Adenine	Adenosine or deoxyadenosine	Adenosine-5′-triphosphate or deoxyadenosine-5′-triphosphate
G	Guanine	Guanosine or deoxyguanosine	Guanosine-5′-triphosphate or deoxyguanosine-5′-triphosphate
C	Cytosine	Cytidine or deoxycytidine	Cytidine-5′-triphosphate or deoxycytidine-5′-triphosphate
T	Thymine	Deoxythymidine	Deoxythymidine-5′-triphosphate
U	Uracil	Uridine	Uridine-5′-triphosphate

5. ATP is made from adenine, ribose, and three phosphates linked the 5′-hydroxyl of the ribose. dATP is the same, except that the sugar is deoxyribose.

6. The sequence on the opposite strand for each of the following (all read 5′ → 3′) is ACGTAT TGCATA AGATCT TCTAGA ATGGTA TACCAT.

7. They are DNA sequences because of the presence of thymine rather than uracil.

8.

(a) Definitely yes! If there is anything that you don't want falling apart, it's your storehouse of genetic instructions. (Compare the effectiveness of a computer if all the *.exe files were deleted.)

(b) In the case of messenger RNA, yes. The mRNA is the transmitter of information for protein synthesis, but it is needed only as long as a particular protein is needed. If it were long-lived, the protein would continue to be synthesized even when not needed; this would waste energy and could cause more direct detrimental effects. Thus, most mRNAs are short-lived (minutes); if more protein is needed, more mRNA is made.

9. Four different kinds of bases—adenine, cytosine, guanine, and uracil—make up the preponderant majority of the bases found in RNA, but they are not the only ones. Modified bases occur to some extent, principally in tRNA.

10. This speculation arose from the fact that ribose has three hydroxyl groups that can be esterified to phosphoric acid (at the 2′, 3′, and 5′ positions), whereas deoxyribose has free hydroxyls at the 3′ and 5′ positions alone.

11. The hydrolysis of RNA is greatly enhanced by the formation of a cyclic 2′,3′-phosphodiester intermediate. DNA, lacking the 2′-hydroxyl group, cannot form the intermediate and thus is relatively resistant to hydrolysis.

9.3 The Structure of DNA

12.

Structure	Kind of Nucleic Acid
A-form helices	Double-stranded RNA
B-form helices	DNA
Z-form helices	DNA with repeating CGCGCG sequences
Nucleosomes	Eukaryotic chromosomes
Circular DNA	Bacterial, mitochondrial, plasmid DNA

13. See Figure 9.8.
14. Statements (c) and (d) are true; statements (a) and (b) are not.
15. Proponents for the patent system say it takes money to drive research. Companies will not want to invest hundreds of thousands to millions of dollars into research if they cannot get a tangible gain. Opponents believe a patent on what amounts to information stifles more research and even prevents the advancement of medicine.
16. The idea of patenting information began with a landmark case in 1972 when Ananda M. Chakrabarty, a General Electric engineer filed for a patent on a strain of *Pseudomonas* bacteria that could break down oil slicks more efficiently.
17. Two genes related to breast cancer, *BRCA 1 and BRCA 2*. In 2009 a group of patients, doctors, and research professionals brought a suit to invalidate those patents. They argue that the two genes are “products of nature” and should never have been patented in the first place
18. The major groove and minor groove in B-DNA have very different dimensions (width); those in A-DNA are much closer in width.
19. Statement (c) is true. Statements (a) and (b) are false. Statement (d) is true for the B form of DNA but not for the A and Z forms.
20. Supercoiling refers to twists in DNA over and above those of the double helix. Positive supercoiling refers to an extra twist in DNA caused by overwinding of the helix before sealing the ends to produce circular DNA. A topoisomerase is an enzyme that induces a single-strand break in supercoiled DNA, relaxes the supercoiling, and reseals the break. Negative supercoiling refers to unwinding of the double helix before sealing the ends to produce circular DNA.
21. Propeller-twist is a movement of the two bases in a base pair away from being in the same plane.
22. An AG/CT step is a small section of double-stranded DNA where one strand is 5′-AG-3′, and the other is 5′-CT-3′. The exact nature of such steps greatly influences the overall shape of a double helix.
23. Propeller-twist reduces the strength of the hydrogen bond but moves the hydrophobic region of the base out of the aqueous environment, thus being more entropically favorable.

24. B-DNA is a right-handed helix with specified dimensions (10 base pairs per turn, significant differences between major and minor groove, etc.). Z-DNA is a left-handed double helix with different dimensions (12 base pairs per turn, similar major and minor grooves, etc.).
25. Positive supercoils in circular DNA will be left-handed.
26. Chromatin is the complex consisting of DNA and basic proteins found in eukaryotic nuclei (see Figure 9.15).
27. Genome 10K Project proposes to sequence 10,000 genomes in the next 5 years.
28. Negative supercoiling, nucleosome winding, Z-form DNA.
29. It binds to the DNA, forming loops around itself. It then cuts both strands of DNA on one part of the loop, passes the ends across another loop, and reseals.
30. Histones are very basic proteins with many arginine and lysine residues. These residues have positively charged side chains under physiological pH. This is a source of attraction between the DNA and histones because the DNA has negatively charged phosphates: Histone-NH_3^+ attracts $^-O—P—O—$DNA chain. When the histones become acetylated, they lose their positive charge: Histone—$NH—COCH_3$. They therefore have no attraction to the phosphates on the DNA. The situation is even less favorable if they are phosphorylated because now both the histone and the DNA carry negative charges.
31. Adenine–guanine base pairs occupy more space than is available in the interior of the double helix, whereas cytosine–thymine base pairs are too small to span the distance between the sites to which complementary bases are bonded. One would not normally expect to find such base pairs in DNA.
32. The phosphate groups in DNA are negatively charged at physiological pH. If they were grouped together closely, as in the center of a long fiber, the result would be considerable electrostatic repulsion. Such a structure would be unstable.
33. The percentage of cytosine equals that of guanine, 22%. This DNA thus has a 44% G–C content, implying a 56% A–T content. The percentage of adenine equals that of thymine, so adenine and thymine are 28% each.
34. If the DNA were not double stranded, the requirement G=C and A=T would no longer exist.
35. The base distribution would not have A=T and G=C, and total purine would not be equal to total pyrimidine.
36. The purpose of the Human Genome Project was the complete sequencing of the human genome. There are many reasons for doing this. Some are tied to basic research (i.e., the desire to know all that is knowable, especially about our own species). Some are medical in nature (i.e., a better understanding of genetic diseases and how growth and development are controlled). Some are comparative in nature, looking at the similarities and differences between genomes of other species. Our DNA is at least 95% the same as that of a chimpanzee, yet we are clearly different. An understanding of our genome will help us understand what separates humankind from other primates and nonprimates.

37. Human gene therapy has many legal and ethical considerations. Some are moral and philosophical: Do we have the right to manipulate human DNA? Are we playing God? Should “tailor-made” humans be allowed? Some are more scientific: Do we have the knowledge to do it right? What happens if we make a mistake? Will a patient die that would not have died with other treatments?
38. Advantages would be that people could make informed lifestyle choices. A person with a genotype known to lead to atherosclerosis could change his or her diet and exercise habits from an early age to help fight this potential problem and could also seek preventive drug therapies. Disadvantages might involve legal issues over the right to know such information. Employers could discriminate against prospective employees based on a genotype marker that might indicate a susceptibility to drug abuse, alcoholism, or disease. A caste system based on genetics could arise.
39. Because any system involving replication of DNA by DNA polymerases must have a primer to start the reaction, the primer can be RNA or DNA, but it must bind to the template strand being read. Thus, enough of the sequence must be known to create the correct primer.

9.4 Denaturation of DNA

40. A–T base pairs have two hydrogen bonds, whereas G–C base pairs have three. It takes more energy and higher temperature to disrupt the structure of DNA rich in G–C base pairs.

9.5 The Principal Kinds of RNA and Their Structures

41. See Figures 9.19 and 9.24.
42. Small nuclear RNA (snRNA) is found in the eukaryotic nucleus and is involved in splicing reactions of other RNA types. An snRNP is a small nuclear ribonucleoprotein particle. A complex of small nuclear RNA and protein catalyzes splicing of RNA.
43. Ribosomal RNA (rRNA) is the largest. Transfer RNA (tRNA) is the smallest.
44. Messenger RNA (mRNA) has the least amount of secondary structure (hydrogen bonding).
45. The bases in a double-stranded chain are partially hidden from the light beam of a spectrophotometer by the other bases in close proximity, as though they were in the shadow of the other bases. When the strands unwind, these bases become exposed to the light and absorb it; therefore, the absorbance increases.
46. RNA interference is the process by which small RNAs prevent the expression of genes.
47. More extensive hydrogen bonding occurs in tRNA than in mRNA. The folded structure of tRNA, which determines its binding to ribosomes in the course of protein synthesis, depends on its hydrogen-bonded arrangement of atoms. The coding sequences of mRNA must be accessible to direct the order of amino acids in proteins and should not be rendered inaccessible by hydrogen bonding.
48. They prevent intramolecular hydrogen bonding (which occurs in tRNA via the usual A–U and C–G associations), thus permitting loops that are critical for function, the most important being the anticodon loop.

49. Turnover of mRNA should be rapid to ensure that the cell can respond quickly when specific proteins are needed. Ribosomal subunits, including their rRNA component, can be recycled for many rounds of protein synthesis. As a result, mRNA is degraded more rapidly than rRNA.
50. The mistake in the DNA would be more harmful because every cell division would propagate the mistake. A mistake in transcription would lead to one wrong RNA molecule that can be replaced with a correct version with the next transcription.
51. Eukaryotic mRNA is initially formed in the nucleus by transcription of DNA. The mRNA transcript is then spliced to remove introns, a poly-A tail is added at the 3′ end, and a 5′-cap is put on. This is the final mRNA, which is then transported, in most cases, out of the nucleus for translation by the ribosomes.
52. The numbers 50S, 30S, etc. refer to a relative rate of sedimentation in an ultracentrifuge and cannot be added directly. Many things besides molecular weight influence the sedimentation characteristics, such as shape and density.